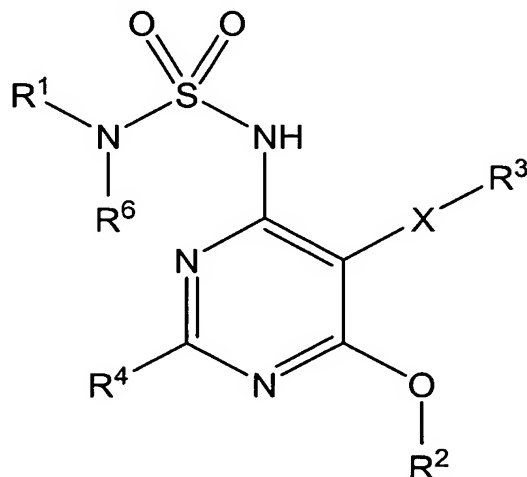


JC17 Rec'd PCT/P10 02 JUN 2005

AMENDMENTS TO THE CLAIMS

1. (Currently amended) ~~Compounds~~ A compound of the general formula I,

**General Formula I**

wherein

R¹ represents lower alkyl-O-(CH₂)_n-, cycloalkyl-O-(CH₂)_n-, cycloalkyl-CH₂-O-(CH₂)_n-;

R² represents -CH₃; R^a-Y-(CH₂)_m-;

R³ represents aryl; heteroaryl;

R⁴ represents hydrogen; trifluoromethyl; lower alkyl; lower alkyl-amino; lower alkyloxy; lower alkyloxy-lower alkyloxy; hydroxy-lower alkyloxy; lower alkyl-sulfinyl; lower alkylthio; lower alkylthio-lower alkyl; hydroxy-lower alkyl; lower alkyloxy-lower alkyl; hydroxy-lower alkyloxy-lower alkyl; hydroxy-lower alkyl-amino; lower alkylamino-lower alkyl; amino; di-lower alkylamino; [N-(hydroxy-lower alkyl)-N-(lower alkyl)]-amino; aryl; arylamino; aryl-lower alkylamino; aryl-thio; aryl-lower alkylthio; aryloxy; aryl-lower alkyloxy; aryl-lower alkyl; arylsulfinyl; heteroaryl; heteroaryl-oxy; heteroaryl-amino; heteroarylthio; heteroaryl-lower alkyl; heteroarylsulfinyl; heterocyclyl; heterocyclyl-lower alkyloxy; heterocycliloxy; heterocyclylamino; heterocyclyl-lower alkylamino; heterocyclylthio; heterocyclyl-lower alkylthio; heterocyclyl-lower alkyl; heterocyclylsulfinyl; cycloalkyl; cycloalkyloxy;

cycloalkyl-lower alkyloxy; cycloalkylamino; cycloalkyl-lower alkylamino;

cycloalkylthio; cycloalkyl-lower alkylthio; cycloalkyl-lower alkyl; cycloalkylsulfinyl;

R⁶ represents hydrogen or methyl;

X represents oxygen; sulfur; -CH₂- or a bond;

Y represents a bond, -O-; -NH-; -SO₂-NH-; -NH-SO₂-NH-; -O-CO-; -CO-O-; -O-CO-NH-;
-NH-CO-O-; -NH-CO-NH-;

n represents the integers 2, 3, or 4;

m represents the integers 2, 3, or 4; and

R^a represents aryl, heteroaryl, lower alkyl, cycloalkyl, hydrogen;

and optically pure enantiomers, mixtures of enantiomers ~~such as for example~~

~~racemates~~, optically pure diastereomers, mixtures of diastereomers, diastereomeric

racemates, mixtures of diastereomeric racemates and the meso-forms and

pharmaceutically acceptable salts thereof.

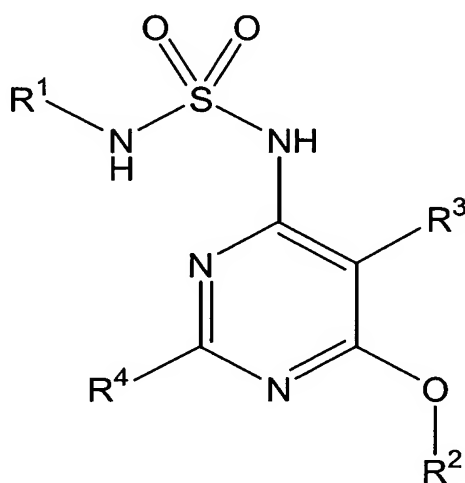
2. (Currently amended) ~~Compounds~~ The compound of general formula I in claim 1, wherein ~~R¹, R², R⁴ and R⁶ are as defined in general formula I in claim 1~~, R³ represents phenyl, mono- or di-substituted phenyl substituted with ethoxy, methoxy or chlorine and X represents oxygen, and pharmaceutically acceptable salts thereof.

3. (Currently amended) ~~Compounds~~ The compound of general formula I in claim 1, wherein ~~R¹, R⁴ and R⁶ are as defined in general formula I in claim 1~~, R³ represents phenyl, mono- or di-substituted phenyl substituted with ethoxy, methoxy or chlorine, X represents oxygen and R² represents -(CH₂)_m-Y-R^a, and pharmaceutically acceptable salts thereof.

4. (Currently amended) ~~Compounds~~ The compound of general formula I in claim 1, wherein ~~R¹, R⁴ and R⁶ are as defined in general formula I in claim 1~~, R³ represents

phenyl, mono- or di-substituted phenyl substituted with ethoxy, methoxy or chlorine, X represents oxygen and R^2 represents $-(CH_2)_2-O-R^a$, with R^a being heteroaryl, and pharmaceutically acceptable salts thereof.

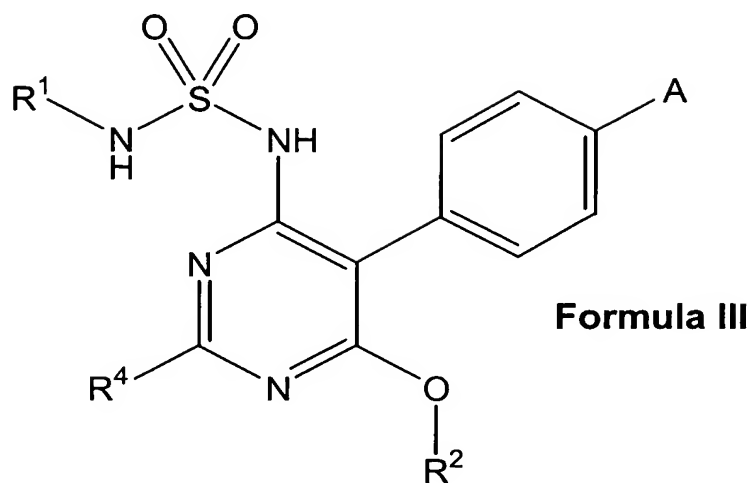
5. (Currently amended) ~~Compounds~~ The compound of claim 1, said compound having formula II



Formula II

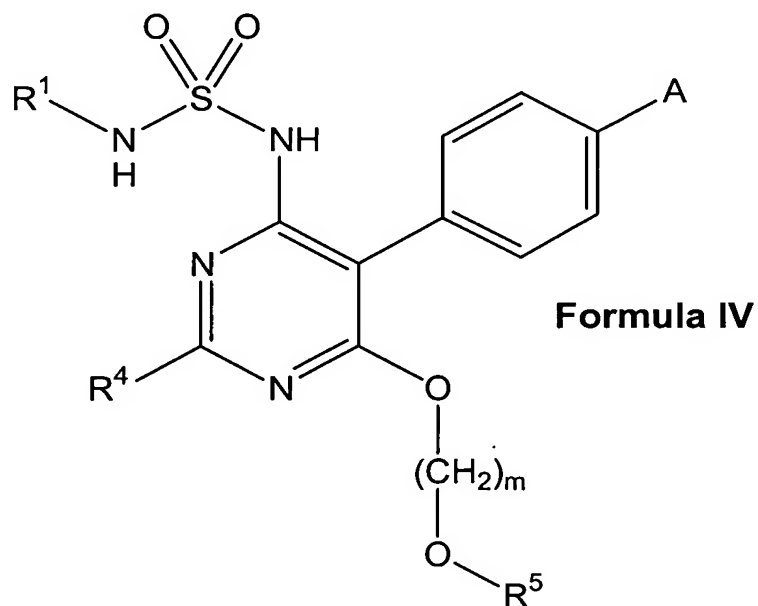
~~wherein R^1 , R^2 , R^3 and R^4 are as defined in general formula I in claim 1, and pharmaceutically acceptable salts of compounds of formula II~~ the compound.

6. (Currently amended) ~~Compounds~~ The compound of claim 1, said compound having formula III



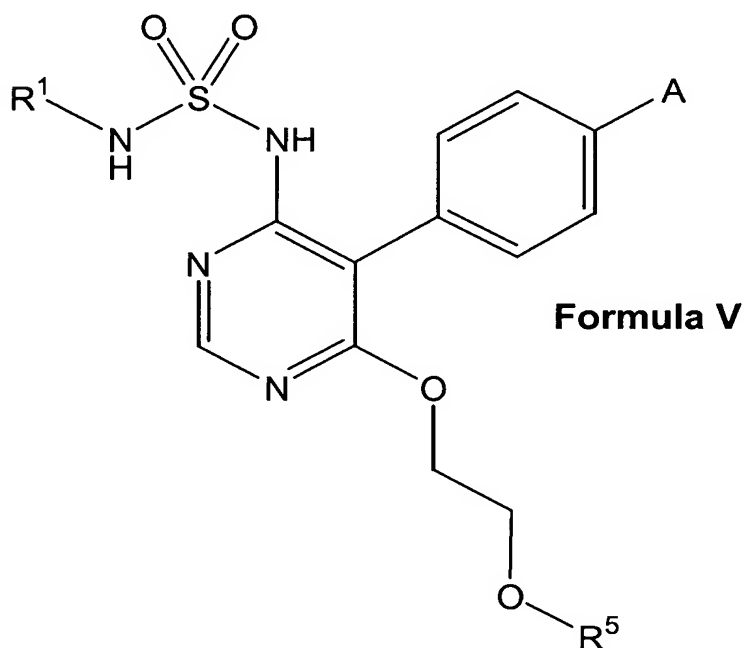
wherein ~~R¹, R² and R⁴~~ are as defined in general formula I in claim 1 and A represents hydrogen, methyl, ethyl, chlorine, bromine, fluorine, trifluoromethyl or methoxy, and pharmaceutically acceptable salts of ~~compounds of formula III~~ the compound.

7. (Currently amended) ~~Compounds~~ The compound of claim 1, said compound having formula IV



wherein ~~R¹, R⁴ and m~~ are as defined in general formula I in claim 1, A represents hydrogen, methyl, ethyl, chlorine, bromine, fluorine, trifluoromethyl or methoxy, and R⁵ represents aryl or heteroaryl, and pharmaceutically acceptable salts of ~~compounds of formula IV~~ the compound.

8. (Currently amended) ~~Compounds~~ The compound of claim 1, said compound having formula V



wherein ~~R¹ is as defined in general formula I in claim 1,~~ A represents hydrogen, methyl, ethyl, chlorine, bromine, fluorine, trifluoromethyl or methoxy and R⁵ represents aryl or heteroaryl, and pharmaceutically acceptable salts of ~~compounds of formula V~~ the compound.

9. (Currently amended) ~~Compounds~~ The compound of formula V claim 8, wherein R¹ is as defined in general formula I in claim 1, A represents hydrogen, methyl, ethyl,

~~chlorine, bromine, fluorine, trifluoromethyl or methoxy and R⁵ represents a substituted pyrimidine, and pharmaceutically acceptable salts of compounds of formula V~~ the compound.

10. (Currently amended) ~~Compounds~~ The compound of general formula I in claim 1, wherein R¹ represents CH₃-O-CH₂CH₂-, and R⁶ represents hydrogen ~~and R², R³, and R⁴ are as defined in general formula I in claim 1,~~ and pharmaceutically acceptable salts of ~~compounds thereof~~ the compound.

11. (Currently amended) ~~Compounds~~ The compound of formula V in claim 8, wherein R¹ represents CH₃-O-CH₂CH₂-, ~~A represents hydrogen, methyl, ethyl, chlorine, bromine, fluorine, trifluoromethyl or methoxy and R⁵ represents aryl or heteroaryl,~~ and pharmaceutically acceptable salts of ~~compounds of formula V in claim~~ the compound.

12. (Currently amended) ~~Compounds~~ A compound selected from the group consisting of:

2-Methoxy-ethanesulfamic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(2-chloro-5-methoxy-phenoxy)-pyrimidin-4-yl]-amide;

2-Methoxy-ethanesulfamic acid {5-(4-bromophenyl)-6-[2-(5-bromopyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl}-amide;

2-Methoxy-ethanesulfamic acid {5-(4-bromophenyl)-6-[2-(5-methylsulfanyl-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl}-amide; and

2-Methoxy-ethanesulfamic acid {5-(4-bromophenyl)-6-[2-(5-methoxypyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl}-amide.

13. (Cancelled).

14. (Cancelled).

15. (Cancelled).

16. (Cancelled).

17. (Cancelled).

18. (Cancelled).

19. (Cancelled).

20. (Cancelled).

21. (Cancelled).

22. (Cancelled).

23. (Cancelled).

24. (Cancelled).

25. (Cancelled).

26. (Cancelled).

27. (Currently amended) A process for the manufacture of a pharmaceutical ~~compositions~~ composition for the treatment of disorders associated with a role of endothelin containing one or more compounds as claimed in ~~any one of claims 1 to 12~~ claim 1 as active ingredients, which process comprises mixing one or more active ingredients with a pharmaceutically acceptable ~~excipients in a manner known per se~~ excipient.

28. (New) A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable excipient.

29. (New) The pharmaceutical composition of claim 28 further comprising one or more other therapeutically useful substances.

30. (New) The pharmaceutical composition of claim 29, wherein the one or more other therapeutically useful substances are selected from the group consisting of α - and β -blockers, vasodilators, calcium-antagonists, ACE-inhibitors, potassium channel activators, angiotensin II receptor antagonists, diuretics, sympatholitics, and prostacyclin derivatives.

31. (New) The pharmaceutical composition of claim 29, wherein the one or more other therapeutically useful substances are selected from the group consisting of phentolamine, phenoxybenzamine, atenolol, propranolol, timolol, metoprolol, carteolol, hydralazine, minoxidil, diazoxide, flosequinan, diltiazem, nicardipine, nimodipine, verapamil, nifedipine, cilazapril, captopril, enalapril, lisinopril, pinacidil, losartan, valsartan, irbesartan, hydrochlorothiazide, chlorothiazide, acetolamide, bumetanide, furosemide, metolazone, chlortalidone, methyldopa, clonidine, guanabenz, reserpine, and flolan.

32. (New) A method for treating or preventing a disorder associated with a role of endothelin, comprising administering to a subject in need thereof a therapeutically or prophylactically effective amount of the compound of claim 1.

33. (New) The method of claim 32, wherein the disorder is a circulatory disorder, inflammatory disorder, or a proliferative disorder.

34. (New) The method of claim 32, wherein the disorder is selected from the group consisting of hypertension, coronary diseases, cardiac insufficiency, renal and myocardial ischemia, renal failure, cerebral ischemia, dementia, migraine, subarachnoidal hemorrhage, Raynaud's syndrome, portal hypertension, pulmonary hypertension, atherosclerosis, prevention of restenosis after balloon or stent angioplasty, inflammation, pulmonary fibrosis, connective tissue diseases, stomach and duodenal ulcer, digital ulcer, cancer, melanoma, prostatic cancer, prostatic hypertrophy, erectile dysfunction, hearing loss, amaurosis, chronic bronchitis, asthma, gram negative septicemia, shock, sickle cell anemia, glomerulonephritis, renal colic, glaucoma, therapy and prophylaxis of diabetic complications, complications of vascular or cardiac surgery or after organ transplantation, and complications of cyclosporin.